United States
Department of
Agriculture

Office of
Agricultural
Biotechnology

Minutes

Agricultural Biotechnology Research Advisory Committee

February 20-21, 1991

Document No. 91-01

U.S. DEPARTMENT OF AGRICULTURE
AGRICULTURAL BIOTECHNOLOGY RESEARCH ADVISORY COMMITTEE
MINUTES OF MEETING
February 20-21, 1991

February 20, 1991

TIME, PLACE, AND PARTICIPANTS

A meeting of the Agricultural Biotechnology Research Advisory Committee (ABRAC) took place on February 20-21, 1991 in Conference Room A, 10th Floor, Aerospace Center, 901 D Street S.W., Washington, DC. The meeting had been announced in the Federal Register and it was open to the public.

Members present included:

Bennie Osburn, Chair, University of California, Davis, CA;
Ann Sorensen, American Farm Bureau Federation, Park Ridge, IL;
Lee Bulla, University of Wyoming, Laramie, WY;
Harold Hafs, Merck, Sharp, & Dohme Laboratories, Rahway, NJ;
William Witt, Food and Drug Administration, National Center for Toxicological Research, Jefferson, AR;
Hugh Bollinger, TerraTek, Inc., Salt Lake City, UT
Frank Whitmore, Ohio State University, Wooster, OH;
John Kemp, New Mexico State University, Las Cruces, NM;
Sue Tolin, Virginia Polytechnic Institute and State University, Blacksburg VA;
Edward Korwek, Hogan and Hartson, Washington, DC;
George Hill, Meharry Medical College, Nashville, TN;
David Andow, University of Minnesota, St. Paul, MN;
Anne Vidaver, University of Nebraska, Lincoln, NE;
David Kline, State University of New York, New Paltz, NY
Alvin Young, Executive Secretary and Director, USDA Office of Agricultural Biotechnology, Washington, DC.

U.S. Department of Agriculture (USDA) Office of Agricultural Biotechnology (OAB) staff present included: Daniel Jones, Maryln Cordle, Martha Steinbock, Marti Asner, Paul Stern, Eva Russnak and Mattie Merritt. Others present are listed in Appendix A.

CALL TO ORDER, APPROVAL OF THE AGENDA AND MINUTES

Dr. Bennie Osburn called the meeting to order at 9:10 a.m. He welcomed members, OAB staff and guests and requested that visitors introduce themselves.

Dr. Osburn asked if there were any suggested changes in the agenda. Dr. Andow suggested that the report on the resources available to support ABRAC and working groups of ABRAC be moved up, so that it would precede discussions of ABRAC working groups. Dr. Young agreed. With this change, the agenda was approved.

Dr. Osburn asked if there were corrections or additions to the minutes of the previous ABRAC meeting. There were none and the minutes were approved as drafted.

USDA GUIDELINES

Dr. Osburn expressed his satisfaction with the publication of the "USDA Proposed Guidelines for Research Involving Planned Introduction Into the Environment of Organisms With Deliberately Modified Hereditary Traits" (henceforth referred to as the Guidelines) in the Federal Register (56 FR 4134, February 1, 1991). He noted that the publication of the Guidelines reflected the diligent efforts of the Committee, OAB staff, and Ms. Zannoni. Dr. Osburn noted that comments on the Guidelines are due April 2, 1991.

Dr. Young conveyed the appreciation of Dr. Charles Hess, Assistant Secretary for Science and Education to the Committee and the previous ABRAC for their efforts on the Guidelines.

Ms. Maryln Cordle noted that the Guidelines published in the Federal Register differed somewhat from those recommended earlier by the Committee. This was due primarily to a two-phase approach the Department had decided to follow. The February 1, 1991 Guidelines represent the first phase providing principles and aid to researchers in the design of their experiments. A second phase will address implementation of the Guidelines.

Ms. Cordle noted that the role of the Institutional Biosafety Committees (IBCs) has changed. The Guidelines as published suggest that principal investigators may wish to seek advice from IBCs and other experts on assessing the safety of a proposed experiment and designing adequate safety protocols. She also indicated minor changes in the Guidelines having to do with scope of oversight and definitions.

Dr. Bulla asked if the Committee could receive a copy of Ms. Cordle's remarks. She agreed to provide them and they are included as Appendix B.

Ms. Lisa Zannoni, in behalf of Dr. Charles Hess, thanked the committee for its thorough work on the Guidelines. She said plans for implementing the Guidelines were being drawn up by an internal USDA task group of senior level people from the Forest Service (FS), the Cooperative State Research Service (CSRS), the Agricultural Research Service (ARS), the Animal and Plant Health Inspection Service (APHIS), and OAB. She presented the committee with a list of objectives of the internal task group (Appendix C). She said the goal of the Task Group is to have a draft implementation package ready by April 2, 1991.

Dr. Korwek noted that the Guidelines are points to consider and not mandatory for USDA funded research. Ms. Zannoni replied

that this is true for the Guidelines now published as principles. However, after the implementation phase, she said compliance with the Guidelines will be required in order to get USDA funding. Ms. Cordle noted that this will require amendment of USDA research funding regulations.

Dr. Korwek asked about the relationship of the Guidelines to existing regulations. He said that originally if a field test was covered by regulation, then it was not to be covered by the Guidelines. Ms. Zannoni said this is still the case. Ms. Cordle put it another way, i.e., if a test is already covered by existing oversight, then the investigator has already complied with the Guidelines. Dr. John Payne, APHIS, said the NIH Guidelines already state that once approval, or other applicable clearance, has been obtained from a Federal agency other than the NIH, an experiment may proceed without the necessity for NIH review or approval.

Dr. George Hill asked about the timeframe for the implementation phase. Ms. Zannoni noted that the Guidelines needed to be finalized based on the comments submitted before implementation could take place. However, the draft implementation packet is being prepared in advance so that implementation can proceed as quickly as possible after the Guidelines are finalized.

Dr. Bollinger inquired about the role of the Competitiveness Council in recommending changes in oversight. Dr. Young replied that the Council normally issues general policy documents which provide a philosophical framework and then government agencies implement those policy statements.

Dr. Bulla asked about the role of ABRAC in the coming months. Ms. Zannoni said ABRAC assistance will be needed in responding to comments. Dr. Bulla asked if the Guidelines and the implementation of the Guidelines being considered are consistent with the recommendations of the Competitiveness Council. Ms. Cordle replied that they are consistent. Dr. Young said he would distribute the Report of the Competitiveness Council to the Committee.

Dr. Kemp noted that implementation was always a part of the ABRAC recommended Guidelines. He asked what will be ABRAC's role in implementation. Ms. Zannoni responded that the internal task group is working from the implementation plan the ABRAC recommended for inclusion in the Guidelines. This plan serves as the starting point for their discussions.

Dr. Young said that the next ABRAC meeting has been tentatively scheduled for May 22-23, 1991. He said that OAB would provide the comments received on the Guidelines to the Committee prior to the meeting. Dr. Vidaver asked if comments received will be considered in the implementation proposal. Ms. Zannoni replied that the comments would not be received in time for the first

draft of the implementation plan, but they will be considered in subsequent drafts.

Dr. Korwek expressed concern that there is not an exact proposal for implementation at this time. He asked if ABRAC will be given the opportunity to review the implementation proposal. Ms. Zannoni said that they would be asked to review the aspects that are ready for public disclosure. This will probably take place at the next meeting.

Dr. Tolin asked what are the correct procedures for ABRAC members to comment on the Guidelines. Ms. Zannoni said comments are welcome from any individual in their personal capacity.

Dr. Jane Rissler, National Wildlife Federation (NWF) said that the NWF is disappointed to see that the principles in the Guidelines have been separated from implementation. She said she did not share the optimism expressed that the implementation phase would be forthcoming quickly. She noted that it has taken 7 years to see the Guidelines published, and that implementation is likely to be a multi-year process which will involve lengthy discussions with OMB. In the interim, no progress has been made. She asked if investigators must now go to NIH for review of experiments?

Ms. Cordle replied that USDA has discussed the review of agricultural research proposals with NIH. The current plan is that USDA will review experiments on a case-by-case-basis until the USDA Guidelines are implemented. Dr. Young added that the Department has the authority to withhold funding if there are unresolved biosafety questions.

Dr. Rissler stated that these procedures and authorities seem nebulous. Dr. Young agreed that some areas are unclear, but he noted that the National Environmental Policy Act (NEPA) provisions which are in place or being put in place by USDA will provide guidance to the Department in the interim.

Dr. Rissler asked if, in the interim, experiments would come to Washington for review. She said she wants to be reassured that safety assurances and procedures for public notice and comments will be in place in the interim. Dr. David MacKenzie, CSRS, replied that all grants submitted to CSRS require an assurance statement which includes such considerations as animal welfare, human subjects, compliance with NIH and other biosafety considerations. He said if a proposal requires public notice, then the public will be involved through the usual procedures. Ms. Cordle added that the NEPA regulations for CSRS are being put in place, but that not all CSRS actions require public comment.

Dr. Rissler asked if the CSRS NEPA regulations will be part of the implementation of the Guidelines. Ms. Cordle replied that

the CSRS NEPA regulations as well as those of other agencies were part of the package.

Dr. Tolin reported that the NIH Recombinant DNA Advisory Committee (RAC) continues to meet and review its role. She said the RAC is considering removing the provisions in the NIH Guidelines which refer to release into the environment.

ABRAC/BSAC COOPERATIVE ACTIVITIES

Dr. Osburn introduced Dr. Lawrence Zeph, EPA Office of Pesticides and Toxic Substances, and Dr. Robert McKinney, Chairman of the EPA Biotechnology Science Advisory Committee (BSAC). He said Dr. Zeph and Dr. McKinney had been invited to the ABRAC meeting to participate in discussions of possible cooperative activities between ABRAC and BSAC.

Dr. Young said that the staffs of USDA and EPA have commenced the development of cooperative relationships. He expressed the view that as the devlopment of biotechnology moves from small-scale testing to larger-scale testing and to commercialization, it will be necessary for the two agencies to work together even more closely.

Dr. Osburn reviewed the role of the ABRAC for the EPA visitors. He outlined the activities the ABRAC engages in to provide advice to USDA and to help ensure that the benefits of biotechnology are brought to fruition while protecting public health and the environment. Dr. Osburn welcomed the BSAC representatives and said the Committee is eager to find ways to work together more closely with the BSAC.

Dr. Zeph thanked Dr. Osburn for the invitation to attend the ABRAC meeting. He stated that BSAC was formed to advise EPA on program areas administrered by the Office of Pesticide Programs (OPP) and the Office of Toxic Substances (OTS), as well as others. He added that EPA research programs such as the bioremediation program may also make use of BSAC. He noted that both offices are formulating new regulations which will provide oversight for microbial products.

Dr. Zeph described the roles of BSAC including the development of advice on scientific issues, product reviews, and regulations. He postulated that providing advice on scientific issues would be a good area for collaboration with ABRAC. He said a subcommittee of the BSAC will review draft EPA regulations in April or May, 1991. A full committee meeting will be held in June or July, 1991 to examine all issues and review the work of the subcommittees over the past one and one-half years. After the full committee meeting there will be additional subcommittee meetings on special issues. There may be topics of common interest which BSAC and ABRAC could examine jointly.

Dr. McKinney stated that both USDA and EPA have a clear challenge to serve the public's needs. He said both agencies must strive to maximize the benefits of biotechnology while minimizing risk. He reported that the 1986 charter of BSAC provides for a committee of 11 members to provide advice to EPA. Nine of the members are scientific experts and two represent public interest groups. He said there are also non-voting members from other Federal agencies who attend BSAC meetings. The BSAC normally meets three times per year to provide scientific advice.

Dr. McKinney said a key issue for the BSAC is how to handle Confidential Business Information (CBI). The committee needs to balance the public's right to know against the need to protect proprietary information. He said BSAC encourages companies to minimize the amount of information classified as CBI. He said this issue may become important for the ABRAC as well in the future.

Dr. McKinney reported that in addition to the parent BSAC committee, there are 15 subcommittees which address specific issues in detail. He noted that there has been valuable public and industry participation in all groups. He said that BSAC and EPA have become involved in international issues. For example, the BSAC reviewed the Good Developmental Practices (GDP) document prepared by the Organization for Economic Cooperation and Development (OECD).

Dr. McKinney described some of the issues recently addressed by the BSAC including releases into the environment, field testing of microorganisms, and greenhouse containment. He noted that the problem of what constitutes a release into the environment remains to be solved. When EPA submitted a definition of release to the EPA Office of General Counsel, it was determined to be scientifically correct, but legally unenforceable. He said this points to the challenge of maintaining scientific accuracy within a regulatory framework. Dr. McKinney concluded his remarks by inviting ABRAC members to attend BSAC meetings and to join in discussions on issues of mutual interest.

Dr. Hafs asked Dr. Zeph and Dr. McKinney to suggest common scientific issues the two committees might work on together. Dr. Zeph suggested the issues of microbial survival and gene transfer might be considered. He also mentioned the possibility of collaborating on reviews of international documents, particularly the document on large-scale releases being prepared for OECD.

Dr. Andow asked how many of the BSAC subcommittees are active. Dr. McKinney replied that many subcommittees are active on paper, but do not meet regularly. Dr. Zeph added that sub-committees on the following topics are active: definition of environmental release; definition of a pathogen; greenhouse containment; minimizing dissemination during field testing,

i.e., confinement; human health effects; antibiotic resistance markers; mobile genetic markers; and bio-geological chemical cycles related to microbial ecological systems.

Dr. McKinney noted that premanufacturing notices submitted to EPA were reviewed by a special subcommittee. He added that there is a need to collect data necessary to support committee decisions. He said that the BSAC has often found that the data required are not available, especially on environmental interactions.

Dr. Andow asked which subcommittees have met within the past nine months. Dr. McKinney replied the subcommittees on health effects, antibiotic resistance markers, mobile genetic elements, and review of the GDP document for OECD have met most recently.

ENVIRONMENTAL ANALYSIS AT THE DEVELOPMENTAL STAGE OF FIELD TESTING

Dr. Osburn introduced Dr. John Payne, APHIS, noting that Dr. Payne has been a regular visitor at ABRAC meetings and contributed to the development of the Guidelines. He thanked Dr. Payne for his contributions.

Dr. Payne preceded his presentation with comments on the minutes of previous meeting. He said the minutes make it appear that he frequently referred to "deregulation", although this is not a term he normally uses. He said more correct terminologies are "adjustment to regulation according to experience gained" and the "need for coordination of regulation." He said he would make his remarks to the Committee within the context of this framework, noting that the issues are not black and white, but rather parts of a complex framework.

Dr. Payne said his presentation would focus on aspects of the regulatory framework, particularly certification mechanisms for reviews as models for flexibility, change, and dynamism. He noted that these concepts are not always associated with regulation, but they are valid. He then presented the history of the APHIS authority to regulate under the Plant Pest Act.

Dr. Payne noted that APHIS has a maximum of 120 days to review an application for a permit. He noted that ABRAC had expressed concern that APHIS may be faced with more reviews than it can handle. However, this has not proven to be the case, he said, because the certification process has built-in flexibility. For example, APHIS is able to grant renewals of permits in cases where applications are substantially similar to previous applications.

Dr. Payne said that many applications received by APHIS are substantially similar to other trials, but differ in a specific way such as different genetic constructs or the use of a new

site within a similar agricultural setting. APHIS reviews these applications and examines the differences between the new and old applications. When the EA is developed the differences are noted, but other aspects of the EA which are unchanged are incorporated by reference. Thus, a completely new review is not needed. Dr. Payne stated that renewals and incorporating parts of EAs for similar tests are adaptions of the review structure which demonstrate its flexibility.

Dr. Payne reported that APHIS is also looking at more fundamental changes in the review process. These include changes in the petition process under 7 CFR 340.4 which specifies the process for granting exclusions from regulation for particular organisms. He said another change to be considered is a proposal to amend the listing of exempt organisms.

He noted that the changes being considered in the APHIS review process demonstrate dynamism. He said that it is often stated that the level of review should be related to the level of risk. In order to achieve this, regulations may need to be adapted through structural modification and differences in approach. He said APHIS will develop classes or groups which require different treatment based on experience gained. This, he said, may allow the agency to move away from the case-by-case approach.

Dr. Andow asked if APHIS would seek suggestions from other agencies. Dr. Payne replied that this is already taking place. Every EA states what APHIS finds to be important and is available so that anyone can provide feedback including comments on the conclusions reached. The feedback received provides guidance to APHIS. Dr. Payne added that as APHIS plans structural changes in its review process, it would like to have ABRAC and BSAC advice. The agency would also welcome public comments on structural changes.

Dr. Hafs asked if APHIS regulations also cover animal pests. Dr. Payne said that the APHIS regulations which deal with animal biologics are product-oriented. There is a different procedure for these products. He said he had not covered this in his presentation because it is difficult to mix descriptions of the Plant Pest Act with descriptions of regulations covering animal biologics.

Dr. Andow asked Dr. Payne if he could give some indication of the timeframe involved with structural changes in APHIS reviews. Dr. Payne said changes will be made within two years at the outside.

Dr. McKinney asked if Dr. Payne was referring to changes in the APHIS implementation of NEPA or other regulations. Dr. Payne said NEPA is involved, noting that APHIS has reached a Finding of No Significant Impact (FONSI) on each permit. Dr. McKinney

said NEPA is important and that APHIS should be commended for its approach.

Dr. Sally McCammon, APHIS, began her presentation with comments on the process APHIS uses to certify small-scale field tests. She expressed the view that the function of research is to develop new products which contribute to the gross national product. She said APHIS views its regulatory role as technology transfer, as well as protecting the public. She noted that many new crops and crop-associated microorganisms are being developed with the transfer of a variety of genes.

Dr. McCammon reported that the number of basic research institutions taking part in field testing is growing. As of February 4, 1991, she said, APHIS had 45 permits pending of which 12 involve basic research institutions.

Another trend Dr. McCammon reported is that tests are increasingly taking place in multiple sites, and often in multiple states. She interpreted this as evidence that some crop varieties are nearing commercialization.

Dr. McCammon reported that APHIS is preparing a users guide to biotechnology permits. It will contain questions and answers about the permitting process and examples of completed permit applications which will be described in detail.

Dr. McCammon said that APHIS considers a number of factors in preparing the EA for each field test. These include the biology of the organisms, the molecular biology of the transformation, the safeguards proposed by the investigator, proposed confinement, potential for gene transfer, proposed mitigation procedures, and the potential consequences of the organisms on the field test site. She said APHIS certifies that researchers do what they indicate they plan to do in their applications.

Dr. McCammon then described to the Committee the approach APHIS is taking to the developmental stage of field testing. She said that APHIS prefers not to use the term "large-scale" because it implies that it is the opposite of small-scale, which is not the case. Small-scale testing through performance testing is really a continuum.

Dr. McCammon said that the issues involved in the developmental stage of field testing are been addressed in a series of conferences sponsored by APHIS. One conference has already been held on oilseed crucifers. This workshop, which involved 20 panelists from a variety of disciplines, looked at the potential and the consequences of gene transfer as well as other issues including weediness. The participants examined whether safeguards are possible or necessary. She said the experts could not agree on which genes posed a risk if transferred from crucifers. However, there was concern expressed that increasing fitness may result from some field tests. The panelists concluded that

crucifers were highly outcrossing and that gene transfer to Brassica relatives outside the plot is likely.

Dr. McCammon noted that in the applications for the developmental stage, as in the small-scale applications, the safeguards are designed by the applicant, not mandated by APHIS. This is because the purpose of every field test is different and approaches must vary in order to be effective. Safeguards against gene transfer may be biological, physical or temporal.

Dr. McCammon noted that one issue to be resolved is the data necessary to apply for exemption from the APHIS review process. The data requirements for developmental testing may include genetic stability of the new genes, a detailed description of the vector system, the nature of the gene and donor organism, and potential for weediness.

Dr. McCammon described a difference in the way risk is viewed in the U.S. and in Europe. She explained that APHIS views risk as the mathematical product of hazard and exposure. Mathematical modeling techniques can be used to determine risk using this formula. She contrasted this with the view in the European Community (EC) in which risk is viewed as equaling hazard.

Dr. Hill asked if APHIS has noted any special issues which concern academic researchers. Dr. McCammon said that some academic researchers don't understand the permitting system. She also said that many IBCs are unwilling to look at a proposed field test until after the permit is issued. Mr. Terry Medley noted that there has been a trend toward more academic involvement in field testing. He said that currently more than one third of the field tests involve academic researchers.

Dr. Osburn asked about the APHIS regulation of animal biologics. Mr. Medley replied that APHIS had issued licenses for 42 products in this category. He said the APHIS presentation at this ABRAC meeting did not focus on animal biologics, but he noted the United States is the only country to license a recombinant vaccine to date.

Dr. Kline asked why so few of the permits issued by APHIS involve tests of plants with improved nutritional qualities. Mr. Medley replied that the permitting system is externally driven and reflects the applications received. Dr. McCammon postulated there may be technical barriers to transforming the nutritional qualities of plants. She said that the metabolic pathways which control nutritional qualities are more complicated and less well understood than those for single gene traits. She said that companies will develop the easiest and most saleable new products first.

Dr. Kemp asked the APHIS presenters to take a look into the future and try to forecast how plants produced with biotech-

nology will enter the normal commercial market. He asked if new crops would be licensed.

Dr. Medley replied that this is a difficult yet pertinent question. He doubted if commercialization would be like one-stop shopping. He cautioned that plant-pest risk is only one of several issues that might be raised during commercialization of a product. Others, he said, might include herbicidal/pesticidal properties and food safety.

Dr. Kemp noted that traditionally bred Brassica is now grown without permits. He asked how APHIS would handle the commercialization of transformed Brassica. Mr. Medley said this issue had been discussed during a recent meeting with Agriculture Canada. He said APHIS has now received its first application for a small-scale field test of rapeseed, but there are some unresolved issues. Dr. McCammon said the proposed test is being reviewed vis-a-vis the approach taken with non-modified species.

Dr. Korwek referred to the points-to-consider that APHIS had drafted concerning exemptions from the Plant Pest Act. He asked how these points-to-consider will be used. Mr. Medley replied they would be used to determine if organisms could be exempted based on their plant pest risk. Dr. Korwek asked if "unexpected toxicity to humans and animals" was a point-to-consider under the Plant Pest Act. Mr. Medley replied that NEPA covers a broader set of issues than the Plant Pest Act.

Dr. Korwek asked if APHIS intends to consider social and economic factors which may also be encompassed by NEPA. Mr. Medley replied that his agency will not consider social and economic factors. Dr. Korwek asked why APHIS will consider some factors but not others. Mr. Medley replied there is not a requirement for social and monetary evaluations in NEPA. Dr. Korwek questioned that assertion. Mr. Medley reasserted that NEPA calls for evaluation of economic benefit not in monetary terms. He invited Dr. Korwek to review the case law and try to determine what that means. Mr. Medley emphasized that the petition process is open and does not set a standard or license requirement.

Dr. Andow inquired if APHIS would be making any structural changes in its regulations based on the information gathered at the conference on oilseed crucifers. Mr. Medley said that structural changes would be based on data from extensive experience, and that APHIS has only received the first request for field testing rapeseed this year. This proposal will be reviewed on a case-by-case basis. Dr. McCammon noted that the purpose of the conference was not to recommend structural changes in regulations, but to reflect on the issues raised by the developmental stage of field testing crucifers.

Dr. Andow asked how APHIS plans to gather information to support structural changes in regulations. Mr. Medley replied that the

agency is gathering data from many sources including EAs, conferences, and risk assessment research to be carried out in the United States and the EC. Dr. Andow asked how APHIS is exploring possible categories for exemption. Mr. Medley replied that these would result from the petition process which is an open process. Anyone can request an exemption based on data they submit.

Dr. Payne stated that this ABRAC meeting is part of the process APHIS is using to gather information. He said the Agency intends to ask advice from different sources. Getting information from the public is an important part of the process.

UPDATE BY DR. HESS ON THE GUIDELINES, OECD ACTIVITIES AND THE REPORT OF THE COMPETITIVENESS COUNCIL

Dr. Osburn introduced Dr. Charles E. Hess, Assistant Secretary for Science and Education, USDA.

Dr. Hess thanked the Committee members for their work on the Guidelines. He expressed appreciation for their support and the resolution they adopted at the November 1990 meeting. He said USDA is looking forward to receiving comments on the Guidelines.

Dr. Hess said that in order to get the Guidelines published, it was necessary to separate the principles from the implementation phase. He said there is now a USDA task group working on an implementation plan. The goal is to implement the Guidelines and place them in the hands of the research community. He added that as more experience is gained, more exclusions to scope can be added to the Guidelines.

Dr. Hess said he was pleased to hear that the ABRAC is considering the formation of additional subgroups, noting that many worthwhile topics had been proposed for discussion. He expressed an interest in ABRAC discussing what types of expertise should be represented on IBCs.

Dr. Hess reported that USDA has been requested to take the lead in developing a discussion document for the OECD on large-scale field testing. It was noted at the Kiawah Island conference that this is a logical next step in the development of agricultural biotechnology products. He said he has assembled a drafting group which is being led by Dr. Jim Cook, ARS. The first draft of the document should be ready in June 1991. The overall goal of this effort is international harmonization. He said he hoped there would be an opportunity for ABRAC to review the draft document.

Dr. Osburn invited Dr. Hess to comment on the report of the President's Competitiveness Council. Dr. Hess replied that the Competitiveness Council is comprised of Cabinet Secretaries and is chaired by Vice President Quayle. The Council's purpose is

to examine policy issues which affect the economic competitiveness of the United States. A subgroup on biotechnology was formed of which Dr. Hess was a member.

In order to examine biotechnology issues in some detail, the subgroup formed three drafting groups on regulations, science, and financing. Each group worked independently and combined their drafts into the report.

Dr. Hess noted that scope of oversight is one of the issues discussed by the biotechnology subgroup. After the subgroup reached its conclusions on scope, they were presented to Dr. Allen Bromley, who presented them to the Competitiveness Council.

Dr. Vidaver asked if agencies are required to follow the recommendations in the report. Dr. Hess replied that agencies are generally expected to do so. He asked if Dr. Vidaver had a specific point in mind. Dr. Vidaver asked if OMB would follow the recommendations when it reviews documents pertaining to biotechnology. Dr. Hess replied that OMB is expected to do so. Dr. Osburn thanked Dr. Hess for his presentation to the Committee.

REPORTS OF ABRAC PREWORKING GROUPS

Dr. Young reported that the remainder of the ABRAC budget for this year could, under an optimistic scenario, support two full ABRAC meetings and three working group meetings.

Dr. Osburn provided background information on the preworking group reports. He reviewed discussion at the previous meeting leading to the identification of eight possible topics for new working groups. At the previous meeting, he had also asked selected Committee members to develop terms of reference for each of the eight possible working groups. It is these draft terms of reference that he asked to be presented at this ABRAC meeting as preworking group reports.

Dr. Osburn added that ABRAC's role is to advise the Department. Thus, he said, the Committee cannot decide which issues require working group effort. Ultimately, USDA must make this decision.

Mr. Stern provided the Committee with an overview of the process used in developing the terms of reference. He said the preworking group leaders provided him with drafts. He worked with the leaders to organize the material and present it in a more or less standard format. The result of this effort is attached as Appendix E.

The leaders of the preworking groups reported on the draft terms of reference.

Risk Assessment/Priority Setting

Dr. Tolin presented the terms of reference for risk assessment research that she and Dr. Bulla had developed. She noted that they had worked in the context of recommendations of the National Association of State Universities and Land Grant Colleges (NASULGC) and Section 1668 of the Farm Bill of 1990 which provided the legislative authority for a risk assessment research program. She also provided some historical perspective on the role of risk assessment research relative to the NIH Guidelines.

Dr. MacKenzie indicated that the Department will be funding a risk assessment research program, and the proposed working group might suggest what ought to be covered in this program.

Dr. Hess said that he had asked CSRS to carry out the implementation of Section 1668. He said, as of the previous day, a proposal had been submitted to the Administrator of CSRS which outlines options. One option involves targeting the program into areas which support development of the regulatory and review process. One question which remains to be answered is how to select topics. He speculated that certain genetically modified organisms may have priority or it may be preferable to take a model systems approach.

Dr. McKinney stated that the whole subject of risk assessment is a concern to EPA. He said the techniques of risk assessment for field tests are not well understood. Laboratory risk assessment models have been found wanting. He suggested that when applications for field testing are submitted for review there may be opportunities to build-in risk assessment elements. Also, it may be advisable to fund contract research on some of the most pressing issues. There is, he said, a need for program planners in this area to be creative.

Dr. Payne referred to the terms of reference developed by Dr. Tolin. He suggested that categories (a) and (b) be combined and broadened, and that the document might refer to oversight in general rather than solely to the Guidelines.

Ms. Martha Steinbock stated the U.S.- EC Task Force on Biotechnology Research is looking at ways in which the United States and the Commission of the European Communities may be able to work together in risk assessment research.

Dr. Vidaver noted that animals should be included in any risk assessment program. Dr. Tolin agreed.

Dr. Bollinger asked how a non-edible characteristic such as dwarfism in plants would be handled if it is not eaten and is not a pathogen. Dr. Tolin replied that the risk-assessment questions would depend on the identity and use of the product. She added that the considerations would be different for crops

such as tobacco, cotton, trees, and flowers as opposed to food crops.

Dr. Hess noted that there are a number of risk assessment research projects ongoing within the U.S. government. He said that Dr. Henry Habich, EPA, is chairing an interagency group on risk assessment. He suggested that the ABRAC subcommittee communicate with this group.

Dr. Osburn expressed support for the concept of a working group on risk assessment research. He summarized the foregoing discussion noting: there is a funding mechanism available for risk assessment research; there is a demonstrable need for this type of research; the EPA/BSAC is also dealing with this issue; there is a need to develop additional methodologies for outdoor testing; the U.S. - EC Task Force is interested in bilateral cooperation on this topic; and there are other studies being carried out within the U.S. government on this topic.

Data Collection/Database Systems

Dr. Andow reported that the preworking group he led, which included Dr. Osburn, had been formed in response to the Kiawah Island meeting, NBIAP, and other activities which indicated that there are data pertinent to biosafety being generated. The key issue is how to make sure these data are assembled in a useful way. He said assembling these data was necessary if people were to make scientifically-based decisions. Also, a data resource would allow public critics to assess biotechnology more accurately and it would also be helpful to scientists. Dr. Andow then presented the terms of reference for the preworking group.

Dr. MacKenzie stated that he had long supported the collection and organization of biosafety data. He said NBIAP had conducted a survey which involved interviewing the researchers in the U.S. who had conducted field tests. Everyone indicated they would be willing to share biosafety data. An interagency U.S. government group has also recommended developing a data resource in this area.

Dr. MacKenzie identified assessing the need for such a resource as an important difficulty. A full-fledged needs assessment would be very costly. He said he is looking to ABRAC to indicate if there is a need to continue to develop a data resource on biosafety. He said NBIAP is willing to help, but that it does not have the resources to carry out the program on its own. In his view, it would be an expensive operation, but there should be great benefits.

Dr. Kline said someone needs to think about which data are worth collecting and what the database would look like.

Dr. Mark Segal, EPA, referred to the terms of reference prepared by Dr. Andow. He recommended adding a point under 2(c) which would encourage increased interaction with other entities involved with biosafety data collection. He noted that the United Nations Environment Program is interested in developing a global database on the introduction of organisms into the environment and it will sponsor a workshop on this topic in Rockville, MD, March 11-13, 1991.

Dr. Hafs commented that when an experiment is carried out, the data are normally published in a peer-reviewed journal. He asked how the proposed database would differ from this traditional approach and if there is a need to share data more quickly than through the normal publication process. He expressed concern that developing such a database would preclude publishing results in journals.

Dr. MacKenzie responded that biosafety data are often negative results, and that these are not usually published in journals. This is especially true for monitoring data such as data on pollen dispersal that is collected by seed companies during field trials. Dr. MacKenzie asked if APHIS would be interested in better data concerning the distance that pollen travels. Dr. Payne said that APHIS would be interested, but he questioned if the need was great enough to justify a million dollar database.

Dr. Andow said that there is a significant body of "gray" literature worth analyzing. He noted that the approaches to analyzing biosafety data relevant to field testing are in flux. There is not a solid consensus, he said, on how these analyses should be approached.

Dr. Hafs said another way to think of such a database would be to ask if it subsidizes the publication process. He asked if the same arguments for need could not be made for other types of data, for example, data on carcinogenicity which are published in journals. Dr. Hafs noted that quality control of the "gray" literature is a significant problem that needs to be addressed.

Dr. Warmbrodt, National Agricultural Library (NAL), noted that NAL has several semiformal working arrangements with NBIAP. He said NAL is compiling a sophisticated database on biotechnology which could be of help to scientists and others.

Dr. Kemp said he agreed with both sides of the discussion. He noted that APHIS and other agencies are using these data to make important decisions. He said there must be utility in looking at these data seriously. Currently, researchers do not know how to access it.

Dr. Payne reported that APHIS has pertinent "gray" data which it could provide. The challenge is to develop an arrangement in which the data can be provided freely. He said the data is

often semi-privileged, although most of it is not confidential business information (CBI). But, he cautioned, the data may not answer all the pertinent questions. He said data in EAs might be better suited to the purposes being discussed by the Committee.

Dr. MacKenzie said that NBIAP is about to release an artificial intelligence system which will assist researchers in writing applications for permits for field testing. He said a second step is needed in which researchers who have conducted field tests feed their biosafety data into a system. A third step would be risk assessment research on tough questions.

Dr. Hill asked what the value of a data resource would be for industry. He said he did not have the sense that there is an urgent need for this resource. Dr. Witt said that in the case of animal experiments, particularly with regard to toxicity testing, there is a need for a means of determining if such tests have been conducted elsewhere in order to avoid duplication.

Dr. Tolin posed the question of what the ABRAC can do in regard to the database issue which is unique. She argued that the ABRAC contribution should be tied to the USDA Guidelines which may need to be revised as new results on biosafety are generated and analyzed.

Regulatory Relaxation/Harmonization

Dr. Vidaver presented the terms of reference for this preworking group. She acknowledged that Dr. Korwek, Dr. Kemp, Dr. Bollinger, and Mr. Stern had contributed to the terms of reference. The group recognized, she said, that a certain level of regulation is necessary, but members asked if there should be some movement toward deregulation. She said the group divided the topic into two issues, i.e., deregulation which would involve amending legislation or statues, and relaxation which is an internal agency process. Dr. Vidaver framed the main question as whether there is sufficient information to support either approach at this time. She said the group concluded that the answer is yes.

Dr. Vidaver noted that APHIS sees difficulties in internally driven regulatory relaxation. Internal moves for relaxation might be perceived as a conflict of interest by regulatory agencies. She said the question left unanswered at the Kiawah Island conference is when is enough enough. In other words, how often and how many EAs must be written until they are no longer necessary for some organisms?

Dr. Vidaver added that oversight is really a very broad set of activities ranging from standards of practice through local oversight to Federal regulations. She said one area where relaxation may be appropriate is in the discovery phase of

research. Most laws and statutes deal with products, but, in her view, the issues are quite different during the early stages of research.

Dr. Vidaver said if the Committee believes it should play a role, there are number of options for how to proceed. These include drafting petitions for exemptions to submit to APHIS, reviewing petitions, interagency activities such as cooperating on reviews, and other activities. There are some areas not currently regulated, for example, the unique area of fish research.

Dr. Korwek expressed support for the concept, but he suggested it might be improved by making the terms of reference more neutral. He asked if this type of activity is consistent with the ABRAC charter. Ms. Cordle said that she and Dr. Young had met with Mr. Ken Cohen, Office of the General Counsel (OGC), concerning this issue. Mr. Cohen, she said, did not feel that the charter in any way barred the Committee from advising the Department on regulatory issues. The charter includes a broad statement that, in his view, provides sufficient latitude for the Committee in this area.

Ms. Cordle said that it had been suggested that ABRAC could petition APHIS for exemptions to regulations. However, she said, a more appropriate role might be for the Committee to advise USDA on specific organisms the Committee believes should be exempted. The Committee could evaluate if there is sufficient scientific evidence to support a change in regulations. ABRAC could also collect data and review data in support of such changes.

Ms. Cordle said the Department could request that ABRAC take on these areas of consideration. However, she cautioned, the Department would be requesting ABRAC advice rather than asking the Committee to become a petitioner to a regulatory agency. It is ultimately up to USDA and its agencies, she said, to decide what is appropriate and what are the most important topics to be considered. Since different parts of the Department would be affected by ABRAC recommendations on regulatory relaxation, there would need to be a consensus within the Department on what tasks ABRAC should consider in this area. Ms. Cordle said her personal opinion is that OAB should work closely with APHIS and other agencies to determine what approach would be the most effective.

Dr. Korwek posed the question of what activities such a working group would undertake. The goals set forth in the terms of reference, he said, are rather ambitious. Normally, in Dr. Korwek's view, the Committee would submit advice or recommendations to the Assistant Secretary who, at his or her discretion, would forward the recommendations to the rest of the Department. The issues surfaced by this process would then become policy matters. ABRAC thereby has to work through the

USDA policy apparatus. In Dr. Korwek's view, this may limit what the Committee can do.

Ms. Zannoni confirmed that advisory committee recommendations are viewed as advice to the Assistant Secretary.

Dr. Kline asked if discussion of deregulation is premature. He pointed out that the Guidelines are not yet finalized, and the research community may have to conduct more experiments before deregulation is appropriate. Dr. Vidaver replied that the terms of reference under consideration were drafted with APHIS and EPA regulations in mind. There is room for debate, she said, if there is recognition of enough experience at this point to underpin deregulation.

Dr. Vidaver added that discussion of a working group on this topic could be deferred until the implementation plan for the Guidelines has been drafted and made public. Ms. Cordle said that some aspects of the plan may be ready for public discussion in early April 1991.

Dr. Payne described a scenario in which APHIS might ask ABRAC to review selected aspects of its regulatory system. This could be approached operationally, for example, by a request through the appropriate Assistant Secretaries for the ABRAC to conduct a review. Dr. Payne expressed the view that if the Committee took up regulatory issues on its own initiative, it may focus on issues which APHIS has already acted upon and this, in his view, would be inefficient.

Dr. Tolin noted that one option would be for the ABRAC to review petitions.

Dr. MacKenzie reemphasized his concern that few if any individuals or organizations have the resources or the incentive to prepare petitions for broad exemptions under the APHIS regulations. He advocated ABRAC involvement in the petitioning process along with other groups. The question, in his view, was whether the petitioning process should start or end with ABRAC.

Dr. Andow agreed with Dr. Kline that it is first necessary to review the data to determine if there is sufficient evidence for deregulation.

Dr. Korwek asked the Committee to consider exactly what such a working group would do. He said there seem to be divergent views on this topic and that there could be serious procedural problems if the Committee adopts the wrong approach. He said the terms of reference need to be revised.

Dr. Morris Levin, University of Maryland, Baltimore, expressed doubt that enough scientific information is known at this time to justify relaxing regulations in the immediate future. He

added that if the Federal Government moves too hastily to relax regulations this might foster more state regulations.

Academic Field Testing

Dr. Hill presented the report of the preworking group on academic field testing. He reported that it attempted to determine the level of academic activity in field testing. He acknowledged that some private companies engaged in field testing have academic partners, but there appear to be few field tests which are sponsored solely by universities. Currently, of the 48 permit applications pending with APHIS, 13 involve academic institutions and most of these also involve partners in the private sector. Dr. Hill then summarized several topics which a working group in this area might address.

Dr. Kline recalled that the survey conducted by Dr. MacKenzie indicates that many basic research laboratories have organisms ready for testing, but have not yet begun to test outdoors. He added that the survey also indicates the same is true for researchers in the private sector. He concluded that the survey could be a starting point for more detailed consideration of academic field testing.

Dr. Payne recommended that academic field testing be examined in the light of efforts in the U.S. to encourage technology transfer. He suggested that some academic institutions may not be field testing because they have already transferred their research results to the private sector. Often, he said, the rights are assigned before field testing.

Dr. Osburn refuted this suggestion in the area of vaccine development. Traditionally, he said, veterinary schools have supported vaccine development.

Dr. Kemp agreed with Dr. Payne with regard to plant research. Research associated with product development, he said, is too expensive to be carried out by institutions set up to do basic science. He said many public institutions are hired by companies to run trials. Dr. Payne said the same is true for microorganisms being developed as pesticides.

Dr. Tolin agreed, but she pointed out that some research is not likely to be pursued by companies. She cited research related to ecology and risk assessment as examples because, in her view, they are not related to product development.

Dr. Hill concluded that a working group on this topic could make a timely contribution to the development of biotechnology. Dr. Osburn agreed.

Organism Classification/Confinement

Dr. Kemp reported on the preworking group on this topic. He said the preworking group did not wish to revisit the basic concepts developed in the Guidelines. Thus, the terms of reference described a committee to deal with public comments on the Guidelines. He said the preworking group tried to anticipate what topics public comments might address such as need for five classification categories, etc.

Dr. Tolin expressed the view that there is a need for this working group, especially in the area of fine tuning the Guidelines based on public comments. Dr. Osburn agreed that this would be helpful.

Constituency Development

Dr. Sorensen reported on this preworking group which, in her view, had a unique mandate. It was stimulated in part, she said, by frustration over decoupling the principles of the Guidelines from their implementation. At some point, in her view, research policy issues and regulatory policy need to be addressed. One way that implementation of the Guidelines can be assured, she said, is to develop a broad constituency which supports the Guidelines. She posed the question of whether this was needed and referred to the terms of reference for an outline of possible approaches.

Dr. Bulla informed the Committee that he is scheduled to speak at the 5th Annual meeting of the American Society for Microbiology (ASM). He said he intends to describe ABRAC and the Guidelines to the ASM audience. Dr. Kemp said he had already addressed a group in San Antonio on these issues. Dr. Osburn said that he would be addressing an animal health group soon. He asked if OAB could prepare a set of slides which ABRAC members could borrow for their presentations. Dr. Young agreed to do so. Ms. Cordle said that OAB would mail extra copies of the Guidelines to each of the members of the Committee.

Dr. Hill expressed the view that if the Guidelines do not become mandatory, then the constituency group may be increasingly important. Dr. MacKenzie noted that the Guidelines are on the NBIAP system.

Ms. Zannoni asked if the preworking group had addressed the breadth of the constituency which would need to be contacted to support the Guidelines. Dr. Bulla replied that this constituency is very large and that, in his view, the Guidelines should be sent beyond the land-grant system to all academic institutions engaged in research which may be covered by the Guidelines. The Committee discussed how such a broad mailing list could be developed.

Implementation Options

Dr. Whitmore delivered the report of the implementation preworking group. He described what he viewed as the shock of the ABRAC when it learned that the implementation of the Guidelines had been separated from the principles. Dr. Whitmore added that since he now chairs an IBC, he knows first-hand the difficulty IBCs are experiencing in dealing with these issues. Thus, he expressed willingness to work on this group which may help provide them some guidance.

Dr. Whitmore pointed out that the terms of reference developed for this group were drafted before the Guidelines were published. He was also unaware that USDA had an internal task group working on an implementation plan when he developed the terms of reference. He then outlined the options for implementation in the terms of reference.

Dr. Bulla argued that comments received at the 1990 public meetings on the Guidelines indicated that option (d), which states that "the Guidelines be used to evaluate, approve, and exempt field tests...in the manner of the NIH Guidelines" should be strongly considered. He expressed the view that the Committee would be negligent if it overlooked its responsibility to advise the Department on this issue.

Dr. Korwek argued that ABRAC needs to revisit the question of implementation as more information becomes available. He suggested that this working group could review proposals of the Department for consistency.

Ms. Cordle said that since the Department has limited resources to support working groups, the Committee may wish to wait until the in-house task force on implementation finishes its work before recommending the formation of this group. Dr. Young added that the in-house group will present its recommendations to the Assistant Secretary and he may ask ABRAC to review them. Dr. Kemp added that this effort could be incorporated into the other working group which is dealing with the Guidelines.

Dr. Whitmore asked if the in-house task group will focus on the steps necessary to implement the Guidelines. Ms. Cordle replied that Dr. Hess had charged the internal task group with the responsibility of developing a package of actions which will implement the Guidelines.

Dr. Whitmore then concluded, based on this discussion, that a working group on this subject may not be needed.

Food Safety

Dr. Witt recalled that the idea for this preworking group came from the Kiawah Island conference where the question of the use of modified plants as animal feed was raised. He pointed out that no other group appears to be looking at this aspect of the food safety issue.

Dr. Witt posed the question of how an ABRAC working group on this topic would dovetail with existing groups concerned with food safety. He called attention to concerns that FDA may be slow about developing policies on food safety and biotechnology. He said the terms of reference outline possible approaches, the focus of such a group, and the process versus product issue.

Dr. Osburn and Dr. Tolin agreed with the points made by Dr. Witt. Dr. Osburn gave the example of plant waste products such as tomato pumice, orange peels, and cotton seed which are used in preparing animal feeds. He said that if genetically modified plant products are consumed by livestock, there may be concerns about whether this affects animal products used for human consumption. He gave aflatoxin in cows milk as one example. In addition, Dr. Osburn said, the impact of the Bt toxin beyond the host organism may be uncertain once it is broken down and expelled in fecal material.

Dr. Tolin emphasized that food safety is very important. She noted that several international groups are working on these issues, including the OECD. She suggested that an ABRAC working group could either review the OECD document or it could act independently. She expressed the view that the best role for the ABRAC might be to react to existing reports. Dr. Young noted that Dr. Jones of his staff is attending an OECD food safety meeting which is concurrent with this ABRAC meeting.

Dr. Payne distinguished two kinds of food safety issues to be addressed. One is scientific research on food safety which he saw as clearly within the purview of ABRAC. However, he observed that most of the discussion seems to center on regulatory issues. He saw ABRAC activities in the regulatory food safety area as subject to the same constraints that apply to regulatory relaxation/harmonization. Dr. Payne referred to a staff-level interagency committee which meets informally to discuss food safety issues.

Dr. Andow asked if FSIS is examining the issue of feeding livestock plant products produced with biotechnology. Dr. Tolin replied that most of the studies thus far deal with the primary consumption of foods by humans. Dr. Payne replied that the Food and Drug Adminstration (FDA) is responsible for these issues. He indicated that companies are communicating with FDA about specific products and, thus, FDA is informed about products which are to be marketed shortly.

Dr. Frank Serdy, Monsanto, urged the Committee to read and study the report of the International Food Biotechnology Council (IFBC). He expressed uncertainty about whether the report addresses the issue of animal feeds, but he indicated the Center for Food Safety at FDA is examining the report in detail. Dr. Serdy stated that the probability seemed low that food proteins from plants will be passed through livestock and enter the human food supply. Dr. Osburn agreed. He said that this would be relatively easy to prove or disprove through risk assessment research. Dr. Tolin agreed that the ABRAC should study the IFBC report.

Dr. Osburn recessed the meeting until the next day.

February 21, 1991

Dr. Osburn reconvened the meeting at 9:12 a.m. He introduced Dr. Charles Rupprecht of the Wistar Institute, Philadelphia, who gave a presentation on a vaccinia-vectored rabies vaccine field test which he was conducting on Parramore Island, Virginia.

VACCINIA-VECTORED RABIES VACCINE FIELD TEST

Dr. Rupprecht described the scientific objectives of his field test of a rabies vaccine developed for wild animals, primarily raccoons. The rabies vaccine was designed to be administered to animals in the form of bait placed at several locations in the animals' habitat. Objectives of the field test included recording the amounts of bait removed by the animals, quantifying the vaccine uptake by the animals, and assessing clinical signs and/or pathology in the animals. Dr. Rupprecht descibed in detail the experimental protocols for accomplishing these objectives.

Dr. Rupprecht also described the steps he took in obtaining Federal approval to conduct the field test. The proposal for the field test had been reviewed by the USDA Animal and Plant Health Inspection Service (APHIS) which had prepared an environmental assessment and finding of no significant impact under the National Environmental Policy Act. The test began in August, 1990, and was expected to conclude in August, 1991.

In response to a question from the Committee, Dr. Rupprecht gave the approximate annual costs of the field test. He said the research and development phase of the test cost $250,000 to $500,000 per year, the regulatory phase about $500,000 per year, and the conduct of the actual test itself about $800,000 per year. He gave the cumulative direct costs of the test as about $2 million.

Dr. Vidaver asked how long the vaccine is efficacious in animals. Dr. Rupprecht replied that in laboratory studies the

vaccine retained 80 percent efficacy 6 months after vaccination. He also referred to European results in which the vaccine retained some efficacy for up to 18 months following vaccination.

Dr. Osburn observed that the Wistar proposal took about 8 years to gain approval and he asked if Dr. Rupprecht had any recommendations for expediting approval of future field tests. Dr. Rupprecht replied that he regretted some of the public relations aspects of the Wistar field test, but in general, he felt the regulatory environment was becoming less adversarial and more collegial.

Mr. Medley of APHIS pointed out that some field tests, such as those for pseudorabies vaccines, took considerably less time than the Wistar test to gain approval. He referred to 1900 licensed biologic products and recalled that it took 10 staff people and 10 percent of his biologics budget to review the Wistar submission.

Dr. Andow asked how the results of the field test might be affected by the chaotic dynamics of natural populations and by factors of scale. Dr. Rupprecht replied that some of the best rabies models are stochastic in nature. He acknowledged that the dynamics of rabies in raccoons has not been well studied and that his goal is to achieve containment of the spread of rabies first, and then to push back the endemic zone.

Dr. Tolin asked if Dr. Ruprrecht had any contacts with state government other than the Virginia Department of Health. Dr. Rupprecht replied that his team had contacts with the Virginia Department of Agriculture and Consumer Services as well as the Game Commission in addition to the Department of Health.

Dr. Osburn thanked Dr. Rupprecht for his presentation to the Committee.

RHIZOBIUM FIELD TEST AT LOUISIANA STATE UNIVERSITY

Dr. Osburn introduced Dr. Elizabeth Anderson of the Environmental Protection Agency (EPA) to provide background from an EPA perspective on the Rhizobium field test at Louisiana State University (LSU).

Dr. Anderson stated that in 1988 a private firm called Biotechnica International submitted a proposal to EPA for a Rhizobium field test to be conducted on a research farm owned by LSU. EPA and Biotechnica entered into a routine consent order for the conditions of the test including a period of post-test monitoring of the persistence of the test organism. She said that Biotechnica took its final samples in January, 1991, and that the information on persistence of the organism would be submitted to the agency at a later time.

Dr. Kemp asked if the consent order stipulated any field conditions to be maintained by the University after completion of the test. Dr. Anderson replied that, as a noncommercial entity, LSU was not subject to the provisions of the Toxic Substances Control Act (TSCA) and it was not a signatory of the consent order. Thus, the consent order did not stipulate any field conditions to be maintained by the University after the test.

Dr. Osburn invited Dr. Gary Breitenbeck, the principal investigator on the project at LSU, to update the Committee from the LSU perspective. [OAB staff note: Biotechnica International had been notified of the discussion of the field test at this meeting, but the company did not send a representative.]

Dr. Breitenbeck said that Biotechnica had the basic responsibility for engineering the microorganisms. He said that he became involved mainly because of his general interest in Rhizobia and his responsibility for overseeing management of the research farm in behalf of the University.

Dr. Breitenbeck said the overall goal of the field test was to see if nitrogen fixation and soybean yield could be increased by inoculating the soil with the recombinant microorganisms. Six strains of Bradyrhizobium japonica were released: 2 unmodified wild type strains as controls, 2 strains genetically marked for resistance to the antibiotic streptomycin, and 2 strains genetically modified for increased nitrogen fixation with genes from other species of Rhizobia.

Dr. Breitenbeck reviewed the cropping history of the field. It had been planted with corn for 17 years and then left fallow during the previous year.

Dr. Breitenbeck noted that there have been no reported health hazards from B. japonicum. He also noted that all the strains released in the Biotechnica test were morphologically and antigenically similar, they had similar growth rates and persistence patterns, and they were all similar in their abilities to nodulate soybean plants. The immediate goal of the test, he said, was to compare the effects of the inoculant strains on nitrogen fixation and soybean yield.

Dr. Breitenbeck summarized the agronomic results of the field test. He said there were no significant differences in soybean yield attributable to the inoculated recombinant microorganisms. He interpreted this to mean that no response to the inoculants occurred because the indigenous strains of root nodulating bacteria were already meeting the nitrogen requirements of the soybean plants.

Dr. Breitenbeck summarized the biosafety results of the field test. He said there was no evidence of lateral migration of the

recombinant microbes, that there were low levels of the microbes at a soil depth of 25-30 cm, and that no recombinant microbes were found on the control plants. However, he did say that recombinant microbes were found on seeds harvested from the treated plants. From analyses following a heavy rainfall 3 days after planting, he referred to data suggesting that there was on the order of one recombinant microbe per 10 liters of floodwater. However, he acknowledged uncertainties in the plate counts leading to this result because of possible contamination. Otherwise, according to Dr. Breitenbeck, the recombinant strains have successfully colonized the test field and they are persisting.

Dr. Breitenbeck posed a number of research questions that could be pursued concerning the post-release behavior of the recombinant strains. These included whether the recombinant organisms are dispersed into subsoil or groundwater, whether they would colonize other soybean fields, whether there are effective physical mechanisms for dispersal such as seeds, farm equipment, etc., whether native legumes can serve as competent hosts, and whether removal of the domestic host from the field would result in dieback or dieoff of the recombinant strains.

Dr. MacKenzie referred to a letter from the Louisiana Department of Agriculture and Forestry (LDAF) which stated that the LDAF felt that continued monitoring of the field is needed. He said this may represent a unique opportunity to conduct biological monitoring on an organism which is generally regarded as a low risk organism.

Dr. Bulla reviewed several features of the Biotechnica/LSU test. He noted that the field had been replowed thereby blurring the distinction between the test plot and control plot; that the State Department of Agriculture has reservations about feeding the treated soybeans to animals; and that the chairman of the LSU IBC expressed reluctance about reaching a final decision on the matter. In his view, the whole situation raises important questions about the implementation of the research guidelines and since the implementation has not been resolved, the ABRAC may be on soft ground in attempting to deal with the LSU field test.

Dr. Vidaver noted that the ABRAC has essentially no information on the genetic constructs or strains used in the test. If this information is made available and no questions of a biosafety hazard are evident, she saw no problem with ingestion of the seeds by animals or humans, particularly if the seeds are heat processed. She asked how the ABRAC can assist in this effort and in a possible biomonitoring study.

Dr. Kemp expressed clarification on who takes responsibility for the field now that the test is over. He also said that the ABRAC needs a specific proposal for a biomonitoring study before

it can render an informed opinion on the suitability of such a study.

Dr. Whitmore agreed that the LSU test might present an opportunity for the collection of useful biomonitoring information, but he expressed a preference for collecting such information from a better controlled study. He said he might look more favorably on a specific proposal for such a study than on the scant information now before the Committee.

Dr. Andow asked if EPA understood that Biotechnica would pull out at the conclusion of the test. Dr. Anderson replied that Biotechnica's departure was subject to the condition that the company would monitor the field for 18 months after the test and that this was predicated on the perception of a low hazard from the experiment. Dr. Andow questioned the concern about a low hazard experiment and expressed surprise that the issue was appearing before the ABRAC rather than some other component of the Coordinated Framework.

Dr. Korwek expressed confusion about the role of the ABRAC in this issue. He said the release has occurred and there is a de facto assumption that the experiment with this particular organism is safe. He argued that feeding the test seeds to animals is an issue for the Animal Feed Division of the FDA Center for Veterinary Medicine to address.

Dr. Young indicated that the ABRAC had received a written request from the Chairman of the LSU IBC to address this isssue.

Dr. Breitenbeck expressed irritation with the course of events following the conclusion of the field test. He said the guidelines that he has seen are not clear on this issue and a State official with no background in biotechnology is being asked to make a decision.

Dr. Jane Rissler, National Wildlife Federation, questioned the role of the OAB in the absence of guideline implementation and expressed the view that the status of the LSU field following the test was an appropriate matter for ABRAC consideration.

Mr. Terry Medley, USDA Animal and Plant Health Inspection Service (APHIS), reminded the Committee that risk is generally thought of as the mathematical product of hazard and exposure, and that the present discussion has focused on exposure almost to the exclusion of hazard.

Dr. Rissler expressed frustration with the way the Federal government has handled biotechnology issues under the Coordinated Framework (51 FR 23302, June 26, 1986). She contended that the LSU situation is not a question of risk or hazard, but a question of jurisdiction. She faulted the proposed USDA guidelines (56 FR 4134, February 1, 1991) for not

specifying a role for the ABRAC. She said her organization has considered requesting the Department to dissolve the ABRAC.

Ms. Cordle posed the question of the reason for the State quarantine of the LSU test field. She said a representative of the State Department of Agriculture had told her there was reason to believe that the recombinant strains constituted a threat to other plants and the environment. This was, in her view, a difference between State and Federal officials and USDA has mechanisms to handle such situations.

Dr. Kemp asked what EPA would do if the LSU field were a commercial field. Dr. Anderson replied that the test at LSU was approved as a small-scale field test, not as a commercial product, and that EPA might consider a 4 acre field such as that at LSU very differently from a commercial field. She said the consent order with Biotechnica allowed the return of the field to normal agricultural practice if the stipulated control procedures were followed and the post-test monitoring data were collected. She said that EPA has not identified a hazard that would prevent the return of the field to normal agricultural practice.

Dr. Bulla reminded the Committee that agricultural researchers in both Wisconsin and Louisiana are seeking guidance on how they can do their research on low-risk organisms safely. He suggested a discussion of the roles of the ABRAC and the regulatory agencies and the possible development of a memorandum of understanding between USDA and EPA on this issue.

Dr. Osburn noted that decisions on the LSU test have already been made by both EPA and APHIS and he suggested that the Committee consider whether it could endorse these decisions and forward an expression of support to the Administrator of the USDA Cooperative State Research Service (CSRS). To start the discussion, he moved that the ABRAC endorse the statements of EPA and APHIS on the LSU experiment.

Dr. Kemp argued that the ABRAC may not be able to reach an independent endorsement of the EPA and APHIS decisions because it has not had access to the scientific information on the genetic constructs and microbial strains put into the field. He offered an amendment to endorse the agencies' conclusions based on their scientific evaluation.

Dr. Osburn did not disagree with Dr. Kemp's proposed amendment, but he pointed out that ABRAC insistence on seeing the scientific information on the genetic constructs would raise some difficult questions of confidential business information. He suggested the phrase "ABRAC is not in a position to evaluate the scientific information" be inserted into the language of the motion.

Dr. Lawrence Zeph, EPA, indicated that EPA had made a finding of no unreasonable risk from the LSU experiment. If a hazard is demonstrated, he said, the agency has other ways to handle it.

Mr. Medley supported use of the phrase "confidence in the review process" in the ABRAC motion. Ms. Cordle suggested addition of the phrase "ABRAC has seen no information on the genetic construct."

Dr. Breitenbeck said he did not feel obligated to conduct a biomonitoring study and he would prefer to be able to use the field in question as he sees fit in the context of his research program.

Dr. Osburn called a 5-minute recess to draft language for a new motion. Following that, he called for the question on his original motion for the ABRAC simply to endorse the statements of EPA and APHIS on the LSU experiment. The motion was defeated in a vote of 0 in favor and 10 opposed.

Dr. Osburn asked Dr. Jones to read the new motion drafted by Drs. Bulla, Korwek, and Tolin into the record. The motion read as follows: "Although ABRAC is not in a position to evaluate the scientific information that led to EPA's consent order and APHIS's plant pest opinion letter, ABRAC expresses its confidence in the review by EPA and APHIS that resulted in the performance of the subject field release at LSU."

Dr. Andow drew a distinction between confidence in the review vs. the process of review and he prefered to express confidence in the "process of review" rather than a review the ABRAC had not seen.

Dr. Whitmore said the motion pertains to this particular case and he thought expressing confidence in the "review" was appropriate.

A member called for the question and the motion passed by a vote of 9 in favor, 1 opposed, and 1 abstention. Dr. Osburn said the language of the motion would be forwarded to the Administrator, Cooperative State Research Service.

NEW ABRAC WORKING GROUPS

Dr. Osburn indicated that OAB has the staff and funding resources to form no more than 3 ABRAC working groups. He invited views from the Committee on which of the 8 working groups described the previous day should be established.

Dr. Korwek expressed concern about the ABRAC's interagency relationships. He doubted if working groups directed toward regulatory relaxation or food safety would be appropriate for ABRAC. He suggested the idea of a working group on jurisdiction for possible future consideration.

Dr. Vidaver expressed support for a working group on confinement to refine and expand upon the published research guidelines. She acknowledged that many other organizations are already examining biotechnology food safety and that a shift in focus toward feed safety might be appropriate.

Dr. Tolin recommended eliminating working groups on implementation, constituency development, and academic field testing from further consideration.

Dr. Young, on the basis of the ABRAC discussion, proposed the immediate formation of two ABRAC working groups. The first was a working group on risk assessment/priority setting to assist the Department in the area of biotechnology risk assessment research set out in the 1990 Farm Bill. The second was a working group on classification/confinement of organisms to refine the classification system begun by a previous working group and to integrate input from public comments on the research guidelines.

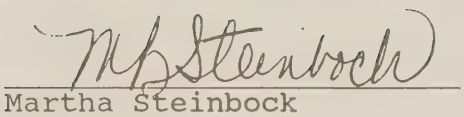
Dr. Young proposed further staff work on two working group concepts with subsequent recommendations to the ABRAC. These were the data collection/database systems working group and a working group on harmonization of oversight as contrasted to regulatory relaxation.

Dr. Kemp moved to establish ABRAC working groups on risk assessment/priority setting and classification/confinement. After a brief discussion, the motion passed by a vote of 10 in favor, 0 opposed, and 0 abstentions.

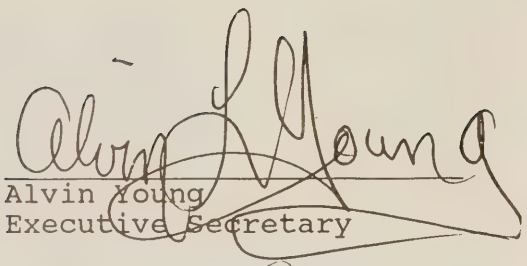
Dr. Osburn asked for volunteers to serve on the newly formed working groups. Drs. Andow, Kline, Hafs, and Bulla volunteered for the risk assessment/priority setting working group. Dr. Tolin was nominated for that working group, but she said her participation would be contingent upon her schedule. Drs. Kemp, Vidaver, Sorensen, Osburn, and Witt volunteered for the classification/confinement working group. Dr. Osburn designated Dr. Andow as chair of the risk assessment/priority setting working group and Dr. Kemp as the chair of the classification/confinement working group.

Dr. Young updated the Committee on several OAB activities and said that OAB would draft a reply from ABRAC to the LSU IBC concerning the Rhizobium test field. Dr. Young announced the dates of the next two ABRAC meetings, May 22-23, 1991, and September 19-20, 1991.

Dr. Osburn adjourned the meeting at 1:12 p.m.

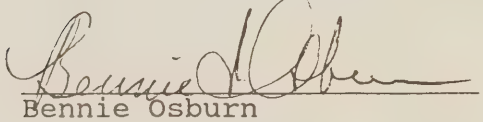


Martha Steinbock
Rapporteur



Alvin Young
Executive Secretary

Daniel Jones
Rapporteur/Editor



Bennie Osburn
Chair

LIST OF APPENDICES

APPENDIX A

LIST OF VISITORS PRESENT

Christopher Plein, University of Missouri
Morris Levin, University of Maryland, Baltimore Campus
David Johnson, Senate Agriculture Committee
Bonnie Buntain, American Veterinary Medical Association
Frank Serdy, Monsanto Company, St. Louis, MO
Ed Bruggemann, National Audubon Society
Roger Jennings, British Embassy
John Payne, USDA Animal and Plant Health Inspection Service
Robert McKinney, National Institutes of Health
Bruce Umminger, National Science Foundation
Lawrence Zeph, Environmental Protection Agency
Marshall Phillips, USDA Agricultural Research Service
Tom Mickle, Select Laboratories, Gainesville, GA
Vergil Davis, Select Laboratories, Gainesville, GA
Grenn Gray, USDA Cooperative State Research Service
Joan Murphy, Food Chemical News
Ray Dobert, Staff of Senator Tom Daschle
Warren Springer, Northrup King, Minneapolis, MN
Janet Shoemaker, American Society for Microbiology
Dave Speck, Staff of Senator Albert Gore
Mark Segal, Environmental Protection Agency
Lisa Zannoni, USDA Science and Education
Jay Blowers, USDA Cooperative State Research Service
Robert Warmbrodt, USDA National Agricultural Library
Sally McCammon, USDA Animal and Plant Health Inspection Service
Terry Medley, USDA Animal and Plant Health Inspection Service
Stuart Auchincloss, George Washington University
Kathy Hudson, U.S. Public Health Service
Michael Broder, Environmental Protection Agency
Scott Shore, North Carolina Department of Agriculture
M.S. Martinez, Embassy of Mexico
Gwen McClung, Environmental Protection Agency
Shirley Ingebritsen, USDA Animal and Plant Health Inspection Service
Jerry LeVeck, Environmental Protection Agency
Jane Rissler, National Wildlife Federation
Louis Kessler, Univax Biologics, Rockville, MD
Charles Rupprecht, Wistar Institute, Philadelphia, PA
Beth Anderson, Environmental Protection Agency
Kay Austin, Environmental Protection Agency
Kathleen Bailey, Environmental Protection Agency
Margaret McLaughlin, U.S. Office of Technology Assessment
David MacKenzie, USDA Cooperative State Research Service
Philip Sayre, Environmental Protection Agency
Gregory Hess, Office of the Secretary of Agriculture

ABRAC BRIEFING - STATUS OF GUIDELINES

Given by Maryln Cordle, February 20, 1991

The Guidelines were published in Part III of the Federal Register, February 1, 1991. (56 FR 4134).

The comment period ends April 2, 1991.

I'll briefly go over how the proposal differs from that recommended by ABRAC.

1. Purpose. The purpose was limited to:

   - Establishing principles for assessing safety and designing confinement to promote safety.

   - The intended use is to aid researchers and institutions in the design of safe experiments conducted outside of contained facilities.

All elements pertaining to USDA use the Guidelines and oversight by IBC's was taken out for later consideration in Phase II, which Lisa Zinnoni will talk about next.

2. IBC role. Section X-B addresses the role of IBCs and other experts, stating

> "Principal investigators may wish to seek advice from IBCs and other expert on assessing the safety of a proposed experiment and designing adequate safety protocols."

However, in the preamble, following a brief discussion of institution's use of IBC's, it says that

> USDA supports these roles for IBCs and requests comments on the use of such committees, adequate membership requirements, and public participation.

It is our intent to consider comments submitted on this item in designing Phase II for implementation.

3. Scope. Another major change is how scope was addressed.

The proposal said the Guidelines were intended for,

"Agricultural research involving the planned introduction into the environment of certain organisms with deliberately modified hereditary traits."

It then said that,

> Appropriate examples will be published, describing the types of environmental research with organisms with deliberately modified hereditary traits for which use of the guidelines is not necessary or appropriate, after comments on the OSTP document are considered together with comments on the guidelines.

In the preamble, the OSTP examples are described, and the exclusions recommended by ABRAC are presented as examples that USDA is tentatively considering.

4. Definitions. Changes were made in the definitions section, mostly eliminating terms no longer used in the Guidelines. Two new definitions were added. These were:

> a. "Deliberately modified hereditary traits" refers to changes to genetic traits of an organism by any method.
>
> b. "Research involving planned introduction into the environment" refers to research outside contained facilities in an appropriately confined environment." Adding that, "It does not refer to the deliberate release of organisms in the open environment beyond research sites or to releases in a commercial setting."

During the public meetings, we were urged by many to make this point clear.

Although the negotiations and Office of Management and Budget clearance process for publication was more protracted than we had hoped for, the outcome in terms of the principles that were published, in my view, retained virtually everything we wanted and is consistent with the ABRAC recommendations.

OBJECTIVES OF THE IMPLEMENTATION COMMITTEE

A. The purpose of the Guidelines is to provide the investigator points to consider in the design of experiments in which genetically modified organisms are to be field tested.

B. The experimental design will be reviewed by an augmented Institutional Biosafety Committee (IBC) which is in the best position to know the investigator and to evaluate potential environmental impacts.

C. The risk level and appropriate containment protocol contained in the experimental design, along with the IBC's review, would be forwarded to the appropriate agency for consideration for funding to provide quality assurance similar to that provided by the NIH Guidelines.

D. The guidelines will include implementation of appropriate exclusions currently being finalized by the Office of Science and Technology Policy.

E. The goal will be to add to the list of exclusions as we gain familiarity with specific types of genetically modified organisms in specific environments. Categorical exclusions should be developed when appropriate.

F. Each agency should explore how compliance with NEPA can be accomplished with minimum effort to both the agency and investigator.

THE ULTIMATE GOAL OF THE GUIDELINES AND THEIR IMPLEMENTATION IS TO PROVIDE THE PUBLIC THE ASSURANCE THAT THERE IS APPROPRIATE REVIEW CONSISTENT WITH THE RISK OF THE PROPOSED RESEARCH AND TO DO SO WITH THE MINIMUM WORKLOAD POSSIBLE UPON THE INVESTIGATOR.

TERMS OF REFERENCE FOR POSSIBLE NEW ABRAC WORKING GROUPS

.1 Risk Assessment/Priority Setting

.2 Data Collection/Database Systems

.3 Regulatory Relaxation/Harmonization

.4 Academic Field Testing

.5 Organism Classification/Confinement

.6 Constituency Development

.7 Implementation Options

.8 Food Safety

University of Florida
INTERDISCIPLINARY CENTER FOR BIOTECHNOLOGY RESEARCH
Agricultural, Medical & Life Sciences

Sheldon M. Schuster, Ph.D.
Director

Jani N. Sherrard
Coordinator

1301 Fifield Hall
Gainesville, Florida 32611

904-392-8408
904-392-8598 Fax
Please reply to:

1022 McCarty Hall
904-392-2356
904-392-8479 FAX

January 30, 1991

MEMORANDUM

SUBJECT: ABRAC Pre-Working Group Discussions

TO: Agricultural Biotechnology Research Advisory Committee

Enclosed are the final draft statements of the suggested work plans for the pre-working groups. Please review these discussions for deliberation during the February 20-21, 1991, ABRAC meeting. It would be helpful to consider the priorities for the various groups in terms of overall needs of the agricultural research community. Please consider whether those needs are being met by other groups, which might make our concentration on those issues redundant or unnecessary. It will not be possible to establish all these working groups at this time. Are there alternative means to achieve the goals of some of the discussions? Would it be possible to combine the goals of some of the discussions into fewer groups? Would it be appropriate to delay concentration on certain issues? At the meeting we hope to decide which working groups should be established and make working group assignments, so we can facilitate swift implementation of these important goals.

Paul Elihu Stern, J. D.
Regulatory Policy Advisor

I. **RISK ASSESSMENT AND PRIORITY SETTING**, January 30, 1991

A. Background

The issue of the risk of biotechnology, real or speculative, has been debated for over 15 years. Numerous conferences, workshops, books, and papers have addressed the issue without reaching resolution on even how to approach the subject. The Congress, in Section 1668 of the 1990 Farm Bill, has directed USDA to conduct risk assessment research and authorized the expenditure of funds for the support of a grant program in that area. As the Department's advisory committee for biotechnology research, it is appropriate for ABRAC to address the nature of this program and to provide advice on priorities.

B. Purpose and Objectives

1. Assist in fulfilling the purpose of ABRAC by providing advice to the Secretary in the area of biotechnology risk assessment.

   a. Examine risk in connection with the Guidelines.

   b. Assess whether recommended confinement conditions for experiments are commensurate with risk.

   c. Recommend research to assess environmental effects of biotechnology.

C. Possible Approaches

1. Review the major approaches that have been used in risk assessment, the results from actual field tests, and the products of workshops and conferences.

2. Explore the validity of the concept espoused in the Guidelines that correlates diminished risk of experiments with increased confinement measures.

3. Examine actual environmental risk that might be measurable by experimentation and an empirical approach.

D. Potential Products

1. Suggestions of priority areas and specific risk assessment experiments to provide results that would:

   a. lead to regulatory relaxation and/or deregulation of research, where appropriate;

   b. lead to increased regulatory stringency, where appropriate;

   c. design and test worst case scenarios empirically under appropriate experimental conditions;

   d. test the validity of using prior experience and familiarity as a prediction of risk;

   e. provide mechanisms for collecting and evaluating data and predicting outcomes of research conducted in the environment.

2. Suggested criteria for grants program requests for proposals and review mechanisms.

I. **DATA COLLECTION/DATABASE SYSTEMS**, January 30, 1991

A. Background and Objectives

The safe and sure development of biotechnological tools and products for use in agriculture requires effective data collection and organization. The availability of data from the testing and regulation of biotechnological tools will:

1. insure informed regulatory decisions and the responsive evolution of regulatory procedures;

2. assure the critics of these tools and potential products that experience is accumulating and being considered in future experimental design and safety review;

3. allow practicing scientists to share data and insights on experimental design of field evaluations so as not to repeat mistakes.

An effective data collection and database management system will provide a means to organize and summarize the information collected during the regulatory process. ABRAC, being a scientific advisory committee, is positioned to assist USDA in the scientific aspects of developing this system.

B. Working Group Charge

1. Define the scientific issues involved in the development of a system of data collection and database management for handling and summarizing the information collected during the regulatory process. This may include:

   a. identification of biological parameters useful in summarizing research results,

   b. specification of theoretical frameworks for the analysis of risk,

   c. classification of cases to allow appropriate comparisons, and

d. determination of significant dimensions of experimental design.

2. Assist and advise USDA in the development of this system of data collection and database management. This may include:

   a. identification of scientific expertise and

   b. interaction with work groups (perhaps oriented around taxonomic groups) that will carry out the actual development process.

I. **REGULATORY RELAXATION/HARMONIZATION**, January 30, 1991

A. Background

Regulation of biotechnology, especially in the area of planned introductions, is viewed as appropriate and necessary for instilling public and commercial confidence about its safety. Many have expected deregulation and regulatory relaxation in the same mode as the requirements of the NIH Guidelines were eased over time. Biotechnological research is regulated in the United States by USDA/APHIS, FDA, and EPA and by some state governments. USDA/APHIS has a mechanism for petitioning for exemptions, but no external petitions have yet been made. USDA/ABRAC has proposed principles for conducting some research and a potential mechanism for decentralized oversight for certain types of discovery experiments.

B. Purpose and Objectives

Agricultural research in the discovery phase should be the scope of this working group. The group should discuss whether deregulation for certain experiments is appropriate and identify, examine, and suggest procedures to implement deregulation.

C. Potential Approach

1. Determine the appropriate role for ABRAC in relation to the federal regulatory agencies.

2. Evaluate the current reach of regulations.

   a. Does the existing experience of the regulating agencies indicate that some experiments should be deregulated?

   b. Is there other evidence that indicates that regulations should be relaxed or removed?

3. Options for the working group:

   a. Establish criteria for and engender appropriate exemption or deregulation petitions or other documents directed at USDA/APHIS, EPA, FDA, or other oversight bodies.

   b. Review petitions of others to be submitted to appropriate regulatory agencies.

   c. Recommend that ABRAC play a role in an interagency review or petitioning body, including research agencies, such as, NSF.

   d. Recommend that ABRAC play no role in deregulation.

4. Potential Products.

   a. A draft memorandum of understanding for ABRAC's role in deregulation to be adopted by participating agencies.

   b. Draft legislation for deregulation.

I. **ACADEMIC FIELD TESTING**, January 30, 1991

A. Background

Of the first 100 field tests of genetically engineered organisms in the United States, less than 10% (nine) were sponsored by the academic community. Institutions represented include Iowa State University, University of Kentucky, Auburn University, University of California, Davis, Pennsylvania State University, and University of Wisconsin. There has been private sector involvement with these, and academic institutions have been involved in private sector research. The academic community has leading scientists who are eager to conduct research which will lead to field testing.

B. Purpose and Objectives

Increased involvement of researchers in projects which would lead to testing of organisms in the environment is both desirable and appropriate. The involvement of the academic community in field testing of new, recombinant organisms is desired and would be beneficial in the advancement of agriculture. Resolving the limitations to academic community field testing will facilitate research efforts and help motivate further important research.

C. Working Group Charge

1. State the importance of academic researchers' involvement in field testing;

2. determine the current level of involvement;

3. identify factors and issues limiting current involvement of academic researchers;

4. identify ways to increase future field testing by academic researchers;

5. describe resources that would be required from the academic, private sector, and government communities to enhance achievement of this goal.

D. The working group should be composed of representatives from the academic community and the private sector with individuals who have interest in achieving these goals.

I. **ORGANISM CLASSIFICATION/CONFINEMENT**, January 30, 1991

A. Background

An important aspect of the evaluation of experimental design involving biotechnological field research is the classification of organisms. The USDA draft guidelines provide a method of such classification and a corresponding method of assigning confinement measures for research design. Examples are included in the appendices which show classification and appropriate confinement for certain organisms and organism groups. These examples and the process they exemplify may require further refinement to engender wide acceptance among the scientific community, constituent organizations, and the public.

B. Purpose and Objective

This working group would be oriented specifically towards an evaluation of the current approach in the USDA Guidelines and providing improvements in the text where appropriate.

C. Questions for Consideration

1. Is there enough information in the current text to guide investigators to design safe experiments? This implies that further refinements will be appropriate after experience is gained with the current text.

2. Are the five levels of safety concern appropriate? Can they be further refined or described at this time?

3. Are the examples of levels of safety concern for organisms adequate? Are more or fewer details needed?

4. Can investigators easily extrapolate from the level of safety concern for the parental organism to determine the level of safety concern for the modified organism?

5. Do the confinement level descriptions in the text need further refinement? Can investigators easily determine the appropriate confinement level from the level of safety concern, or would a different approach be better, e. g., separate points-to-consider documents?

6. Are the organism groups for Appendix 2 appropriate and easy to follow? Are more or fewer groups needed? Are the lists of confinement practices applicable to most research that is likely to be conducted in the near future?

7. Do the lists of confinement practices imply an appropriate level of safety for each of the levels? Should more or fewer practices be presented? Is an appropriate protocol indicated to one who follows the procedure?

D. Charge to the Working Group

1. Examine and evaluate various approaches to refining the classification and confinement provisions of the Guidelines.

2. Recommend specific refinements to USDA to improve the Guidelines.

An example of a modified Brassica napus, carried through all the steps of the Guidelines, is attached as an aid to evaluation of the guideline process. This could provide the working group with a good starting point.

I. **CONSTITUENCY DEVELOPMENT**, January 30, 1991

A. Background, Purpose, and Objectives

The Guidelines will only be of value if people know they exist and believe in the principles they espouse. Regardless of whether or not the Guidelines are published in the FEDERAL REGISTER, it will be helpful to build a wide constituency base to successfully implement them. Development of an active constituency can have several beneficial consequences. Foremost among them, involving groups in the improvement of the guidelines enables them to assume some ownership of the guidelines. This may encourage them to support the implementation of the Guidelines actively. Certainly, if the Guidelines are stalled by the governmental process, active support of a wide constituency base can do a lot to move them along. In addition, because publication of the Guidelines in the FEDERAL REGISTER will not guarantee compliance, the active support of a wide constituency will allow implementation to proceed smoothly. Indeed, if groups critical of the Guidelines can have acceptable responses to their criticisms incorporated into the Guidelines, a very broad support base could be constructed.

B. Possible Approach

1. Identification Stage

Identify:

a. groups that are already aware of the Guidelines and support them (our present constituency base);

b. groups who may not be aware of the Guidelines or who are already aware but critical of the Guidelines (e.g., scientific societies, environmental and consumer activist groups, trade organizations, appropriate state agencies, universities, institutional biosafety committees);

c. reasons why these groups support, criticize, or are unaware of the Guidelines.

d. Mobilization Stage

e. Determine the best means to reach groups who may not be aware of the Guidelines or who are critical of the Guidelines.

(1) personal contacts with directors or heads of societies, trade groups, and environmental groups;

(2) articles and editorials in trade journals and organizational newsletters;

(3) presentations at annual meetings;

(4) articles in USDA publications.

f. Prioritize contacts and set deadlines.

(1) Delegate responsibility for initial contacts.

(2) Maintain computerized, up-to-date records of all contacts in order to allow timely notification of the constituency base concerning changes in the status of the Guidelines.

2. Potential Products

a. A generic explanation of the Guidelines for use in trade journals and newsletters.

b. A generic script with slides or overheads for use in oral presentations.

c. A generic poster display for use at meetings and conventions.

I. **IMPLEMENTATION OPTIONS**, January 30, 1991

A. Background

The original intent of ABRAC in formulating USDA guidelines was to use the structure of the NIH-RAC guidelines as a model. The NIH guidelines are implemented by a system in which certain experiments are exempt from the guidelines; some require approval of the IBC; and some require approval of NIH. Failure to comply with the NIH guidelines may result in loss of research funds from NIH. Other federal agencies have adopted the NIH guidelines, and commercial organizations performing non-NIH funded research with recombinant DNA have voluntarily followed the NIH Guidelines.

B. Purpose and Objectives

The scientific principles for field testing of genetically modified organisms that were developed by ABRAC and OAB have been separated from the implementation procedures. The ABRAC working group on implementation options would make recommendations for use of the Guidelines in a manner that is satisfactory to federal agencies as well as to the research community.

C. Potential Approach

1. Determine the audience for the Guidelines. Who needs the Guidelines? Who is looking for guidance from such a document? Who is trying to avoid implementation of such a document and why?

2. Evaluate the needs of the research community for the Guidelines. Utilize the results of the September 1990 public meetings and other discussions, public and private.

3. Identify options for implementation of the Guidelines and determine the pros and cons of each.

a. Publish the Guidelines in the FEDERAL REGISTER as a source of reasonable, scientifically defensible principles for field testing.

b. Recommend adoption of the Guidelines by USDA in approving research funded by USDA.

c. Recommend incorporation of a process involving IBC review and approval of experiments into the current regulatory process.

d. Recommend use of the Guidelines to evaluate, approve, and exempt field tests of genetically modified organisms in the manner of the NIH guidelines.

I. **FOOD SAFETY**, January 30, 1991

A. Background

The addition, deletion, or other modification of genetic material in organisms that are used for food or feed purposes may raise questions about food safety. Programs and organizations already considering various aspects of the food safety of genetically modified organisms include:

1. Food and Drug Administration (FDA)

2. Food Safety and Inspection Service (FSIS)

3. International Food biotechnology Council (IFBC)

4. Interagency Food Animal biotechnology Information Exchange Group

5. Interagency Coordinating Committee on Food Safety Research

6. Organization of Economic Cooperation and Development (OECD) Working Group on Food Safety

The role of a possible ABRAC working group in this area needs to be clarified in the context of the activities of the above food safety programs and organizations.

B. Possible Approaches

1. Focus on food safety issues that may be unique to research likely to be seen by ABRAC (e. g., growth hormone in transgenic fish).

2. Focus on food safety issues that need to be addressed in agricultural research on genetically modified organisms.

3. Develop criteria for assessing the safety of foods produced through deliberate genetic modification with respect to that of foods produced through conventional genetic modification.

4. Develop more generalized criteria and procedures to evaluate thee safety of products intended as foods or food additives produced through genetic modification.

C. Issues Relevant to Scope of Working Group

1. Will the working group duplicate the work of existing programs or organizations?

2. Are the possible approaches consistent with the mission of ABRAC?

D. Specific Areas for Possible Consideration

1. Potential effects of gene insertion on the regulation of gene expression in the host food organism.

2. Management of selection pressures and development of resistance in disease agents arising from the use of food organisms with engineered disease resistance.

3. Food safety implications of specific types of genetic sequences, marker genes, regulatory genes, etc.

4. Areas of genetic research that might illuminate and/or support the safety of biotechnology-derived foods.

   a. control of gene expression.

   b. tissue- and time-specificity of gene expression.

   c. elucidation of genome maps of food producing organisms.

   d. improvement of genome site-specific methods for insertion, modification, and excision.

5. How does insertion of genetic information affect food quality?

E. Charge to the Working Group

1. Identify specific food safety issues concerning genetically modified organisms that can be addressed at the stage of agricultural research.

2. Develop research priorities for acquiring data to address food safety issues.

* U.S. G.P.O.:1991-281-098:40085/CSRS